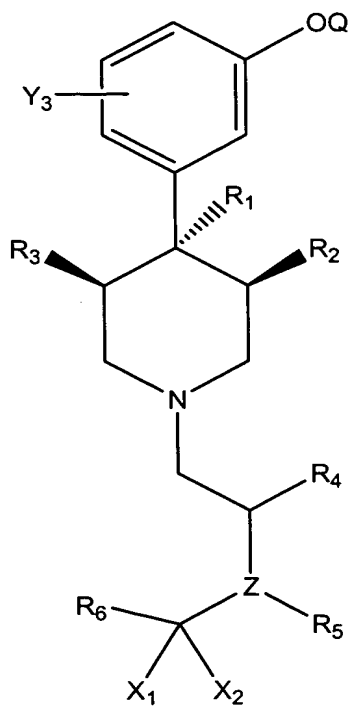


CLAIMS

Please amend the claims as follows:

Claim 1 (Previously Presented): A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

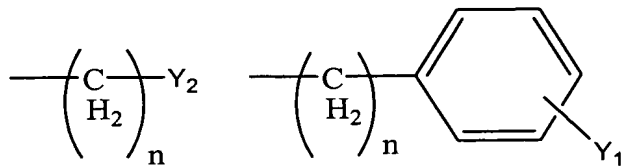
administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (1):

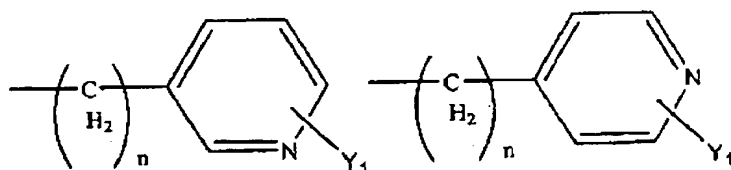


(I)

wherein Q is H or COC₁₋₈ alkyl;

R₁ is C₁₋₈ alkyl, or one of the following structures:





Y_1 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} , alkyl group;

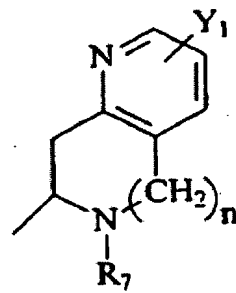
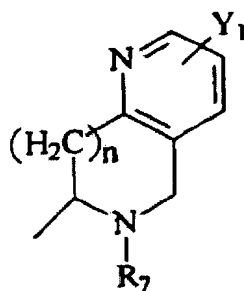
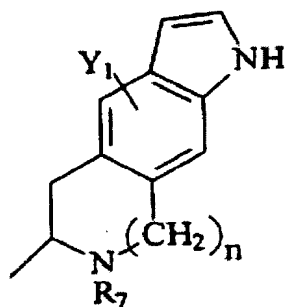
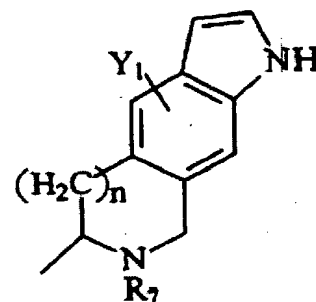
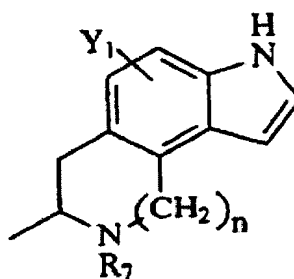
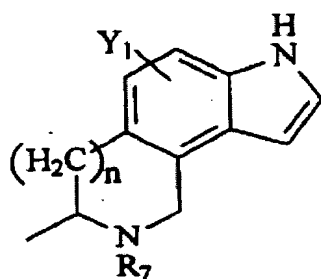
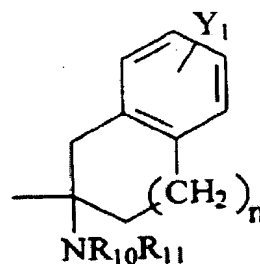
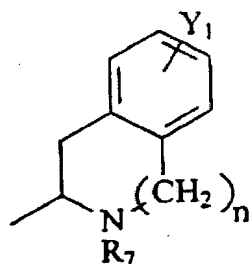
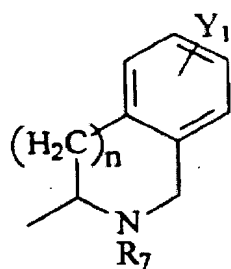
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

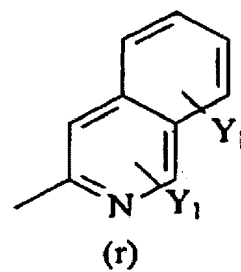
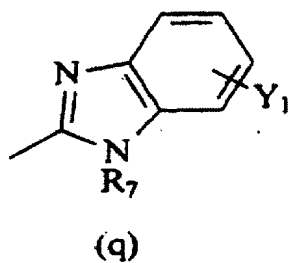
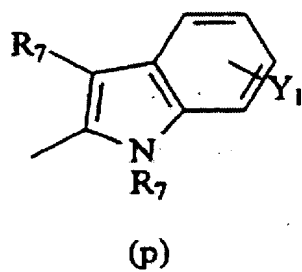
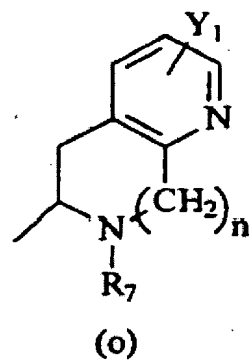
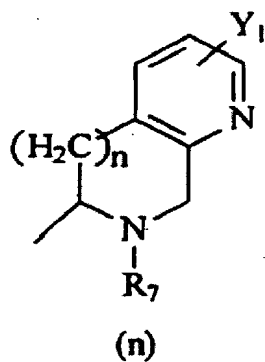
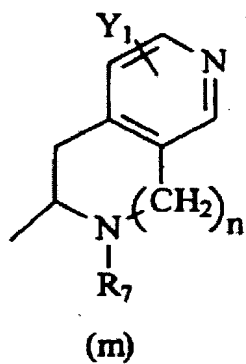
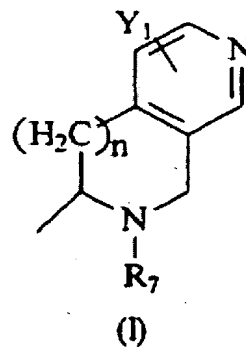
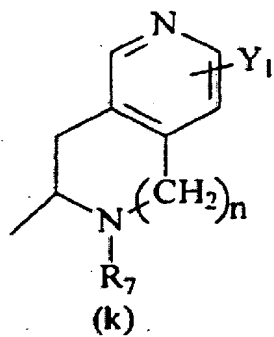
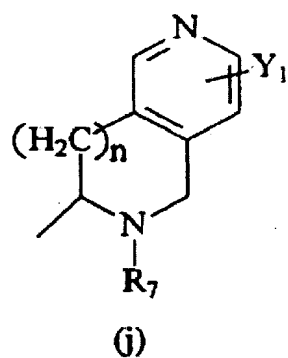
Z is N, O or S; where Z is O or S, there is no R_5

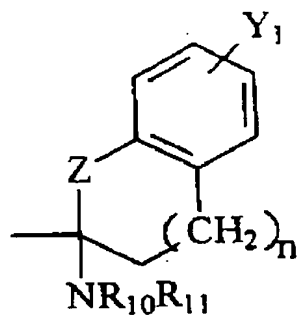
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

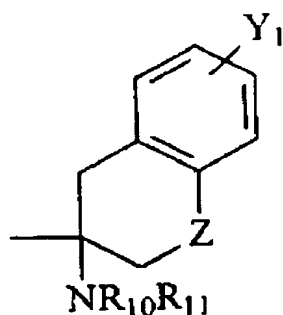
R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



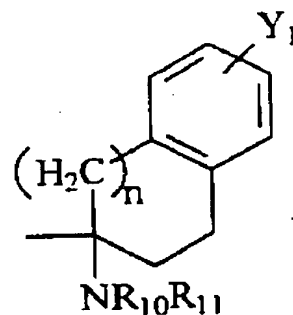




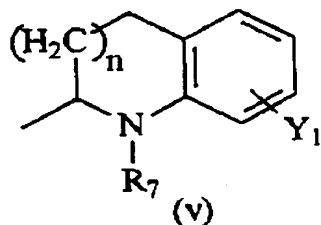
(s)



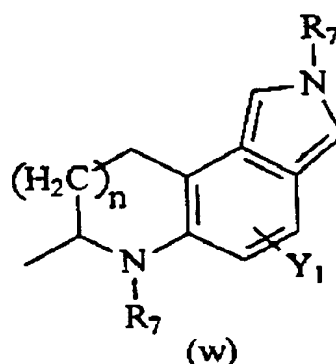
(t)



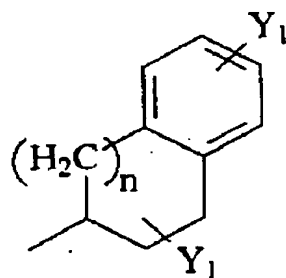
(u)



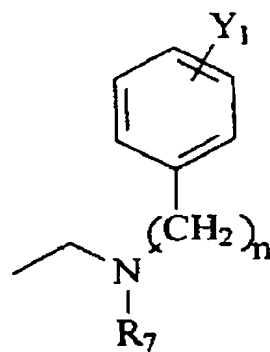
(v)



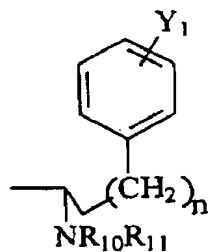
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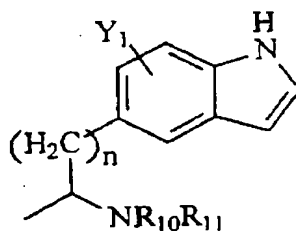
(cc)



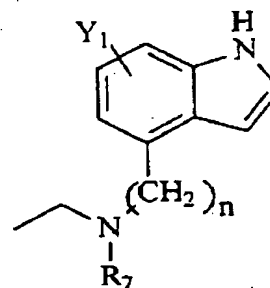
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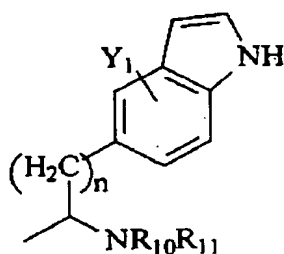
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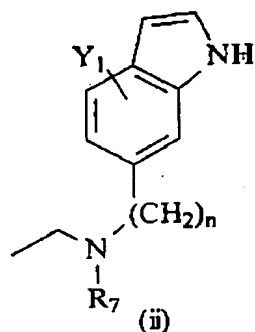
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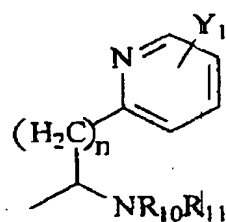
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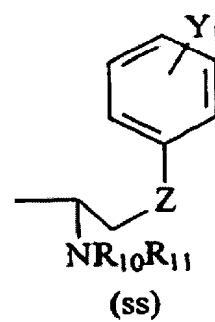
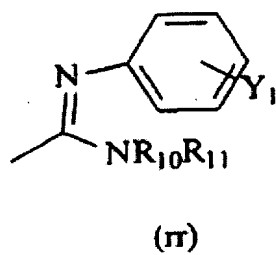
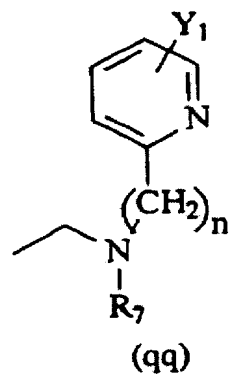
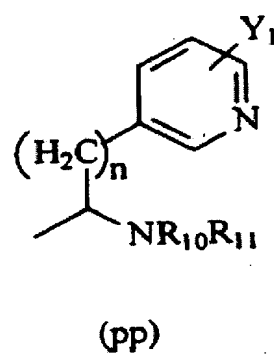
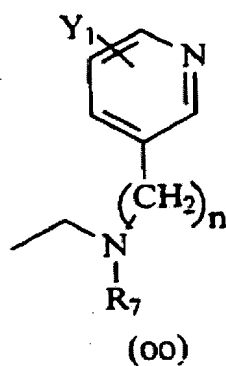
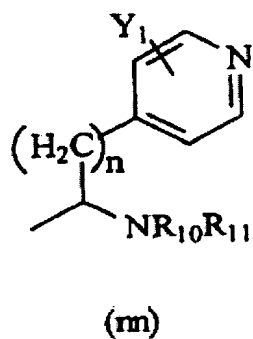
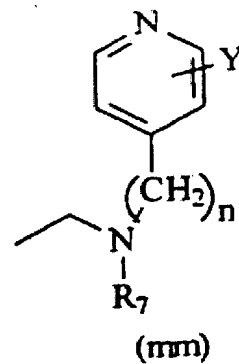
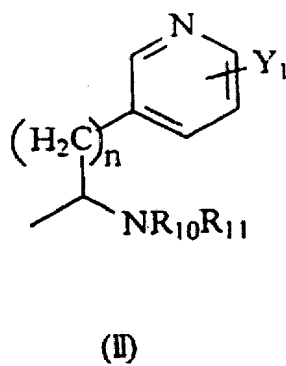
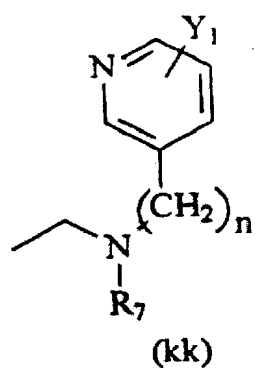
(hh)

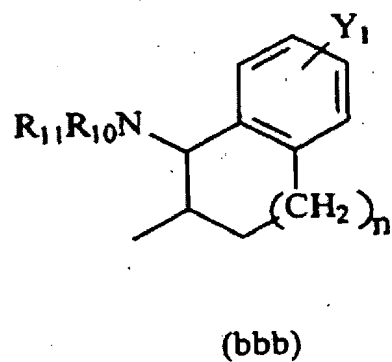
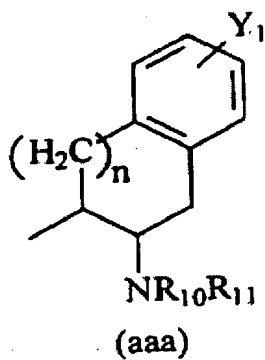
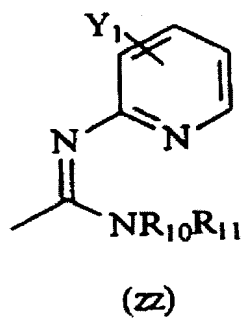
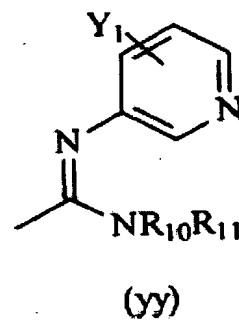
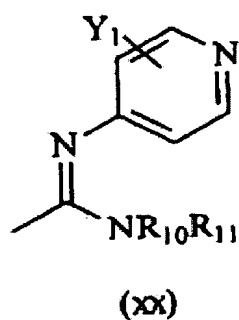
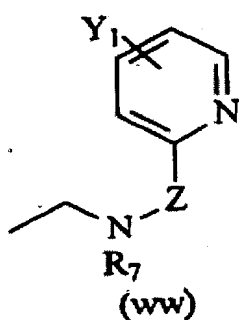
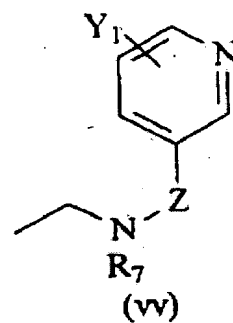
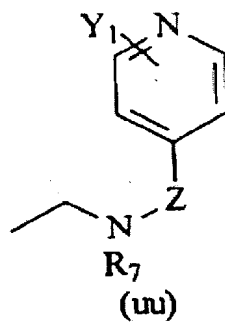
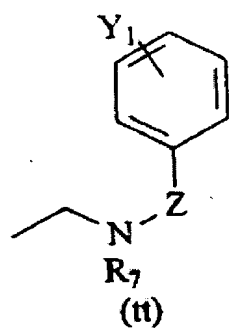


(ii)



(jj)





X₁ is hydrogen, C₁₋₈ alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

X₂ is hydrogen, C₁₋₈alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl; or

X₁ and X₂ together form =O, =S, =NH;

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀, R₁₁,
NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, CH₂(CH₂)_nY₂, or C(=NH)NR₁₆R₁₇;

R₈ is H, C₁₋₈alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₉ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₀ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₁ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₂ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₃ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₄ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₅ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₆ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ; and

R₁₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

and pharmaceutically acceptable salts thereof.

Claim 2 (Previously Presented): The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z , n , X_1 , X_2 , and R_7 - R_{17} are as in Claim 1;

Y_3 is H;

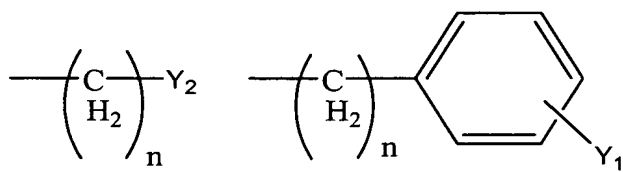
R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkynyl, C_{3-8} alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(w) and (cc);

and pharmaceutically acceptable salts thereof.

3. (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1 , Y_2 , R_4 , R_5 , Z , n , X_1 , X_2 and R_8 - R_{15} are as in Claim 1;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 4 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{15} are as in Claim 1;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, or $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 5 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{14} are as in Claim 1;

R_1 is methyl,

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

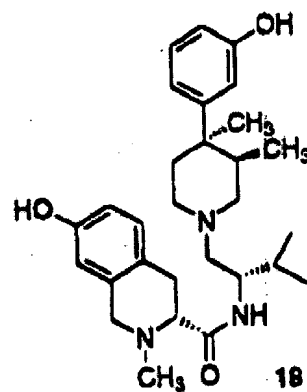
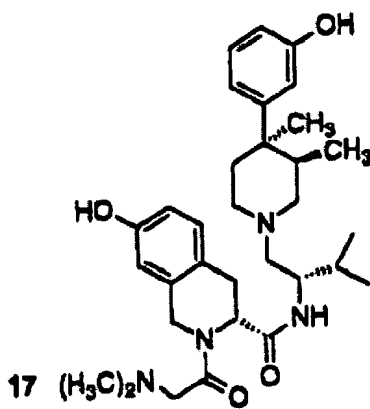
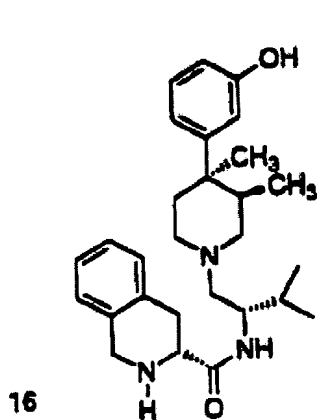
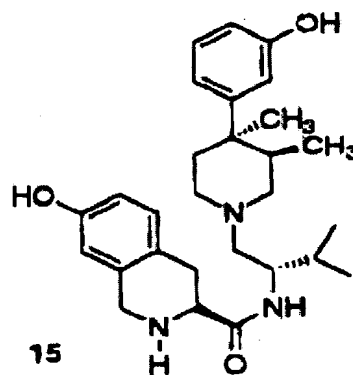
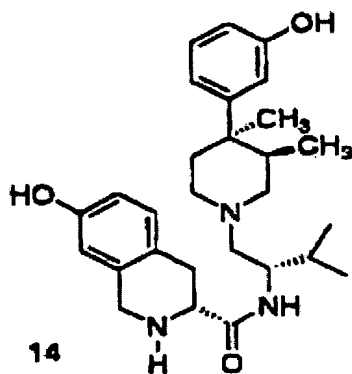
R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

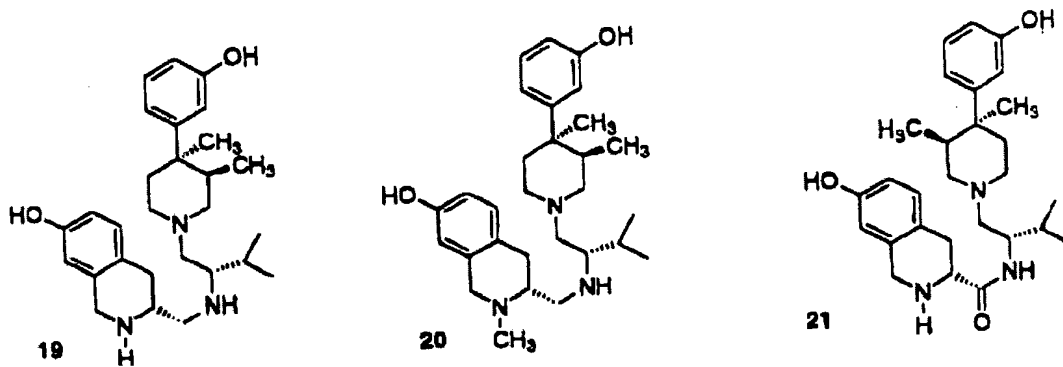
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

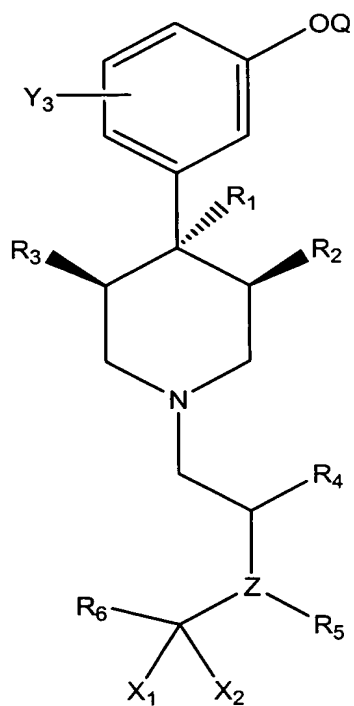
R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

Claim 6 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 as follows:





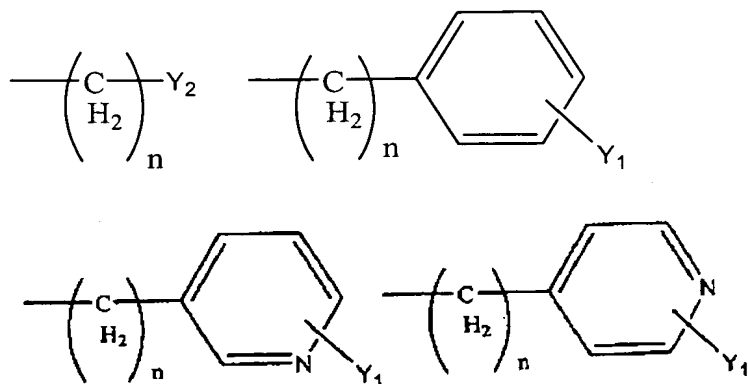
Claim 7 (Previously Presented) A kappa opioid receptor antagonist compound
 represented by the formula (I):



(I)

wherein Q is H or COC₁₋₈ alkyl;

R₁ is C₁₋₈ alkyl, or one of the following structures:



Y_1 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_3R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

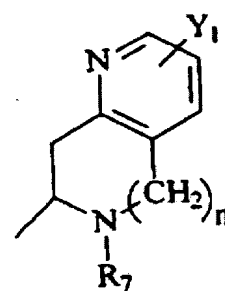
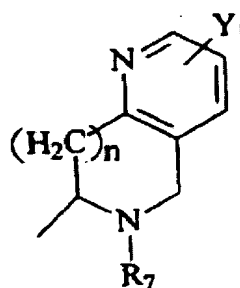
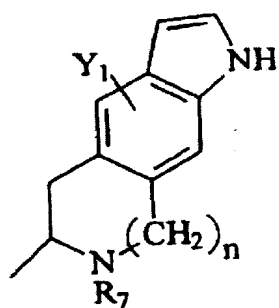
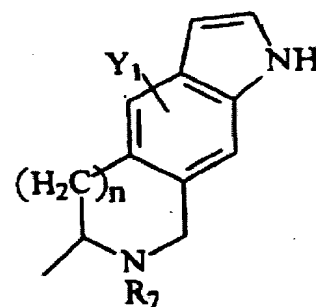
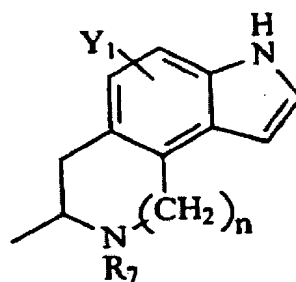
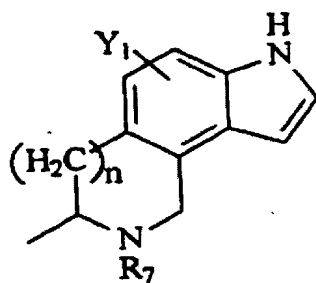
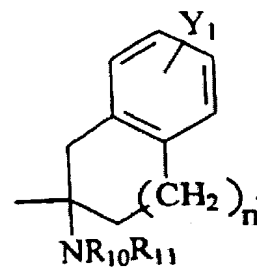
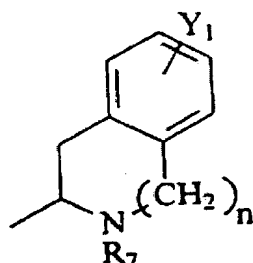
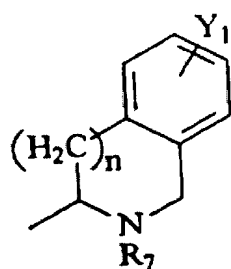
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

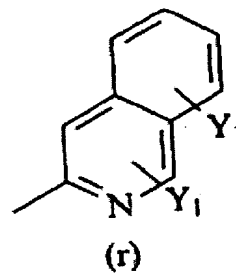
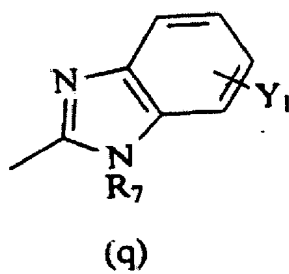
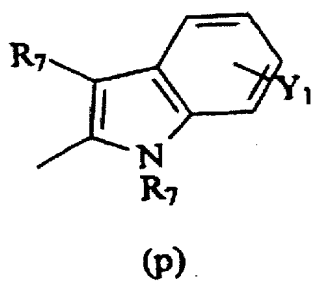
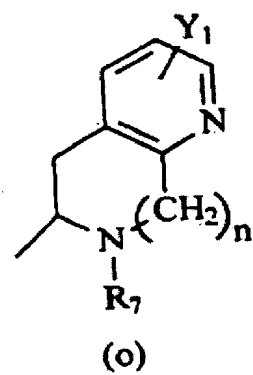
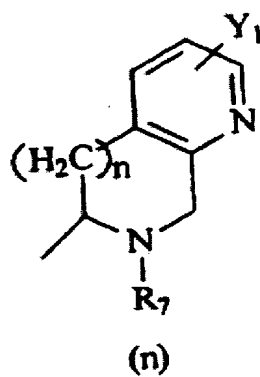
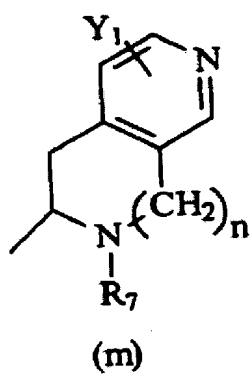
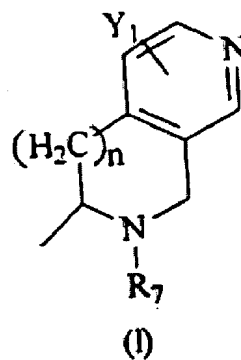
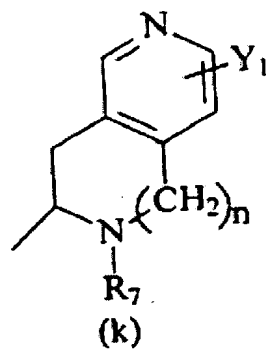
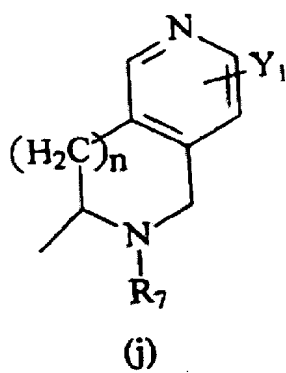
Z is N, O or S; when Z is O or S there is no R_5

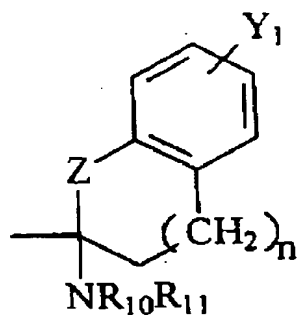
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

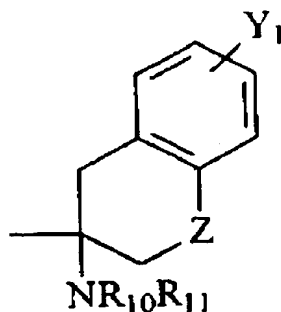
R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



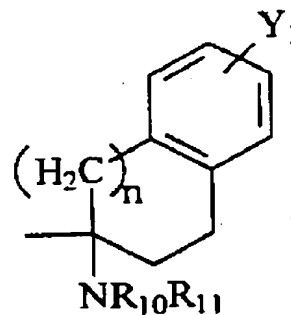




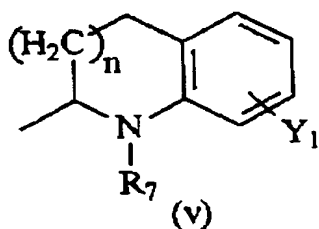
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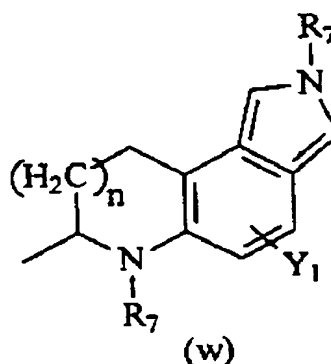
(t)



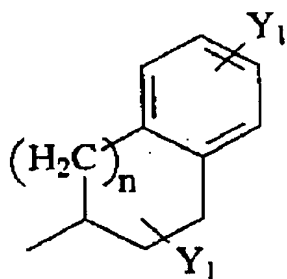
(u)



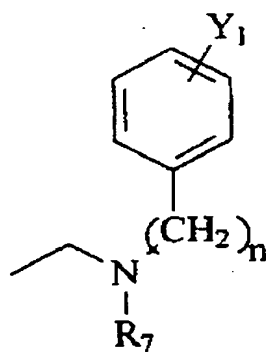
(v)



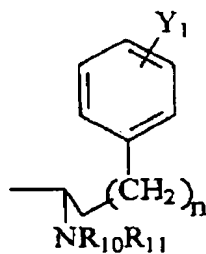
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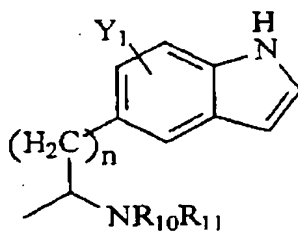
(cc)



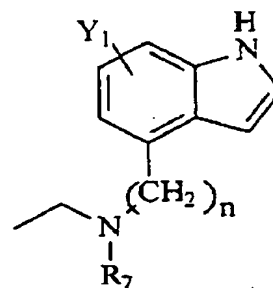
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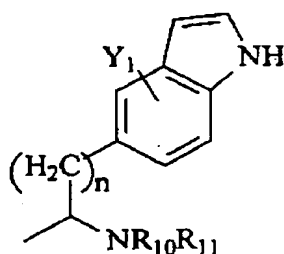
(ee)



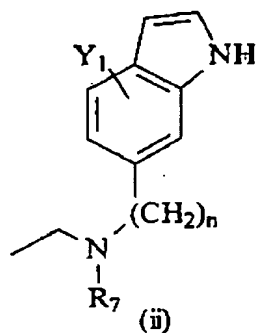
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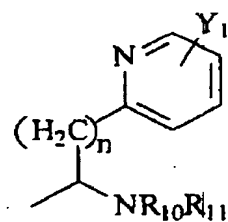
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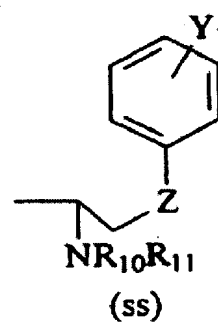
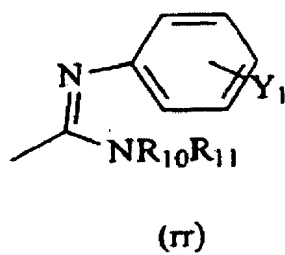
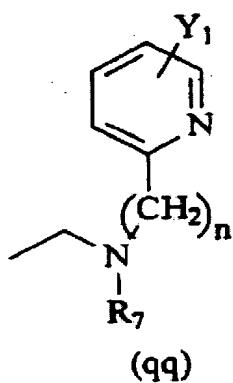
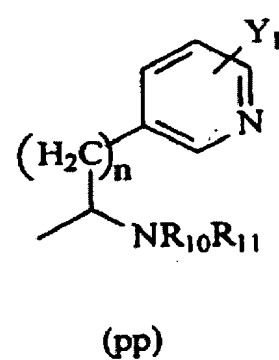
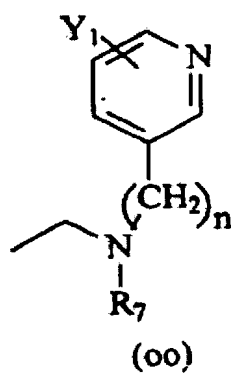
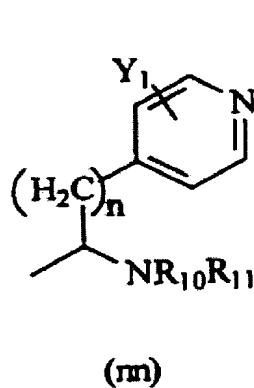
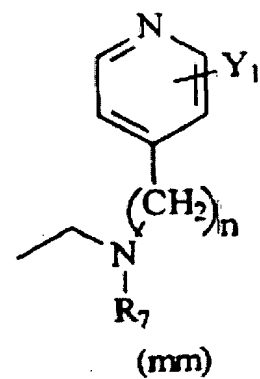
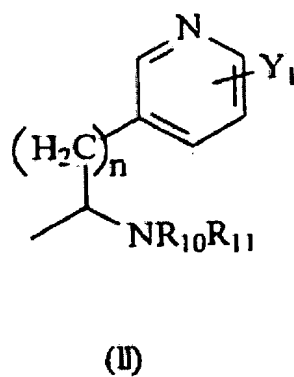
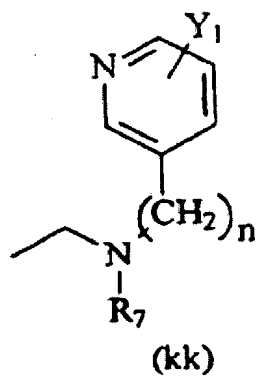
(hh)

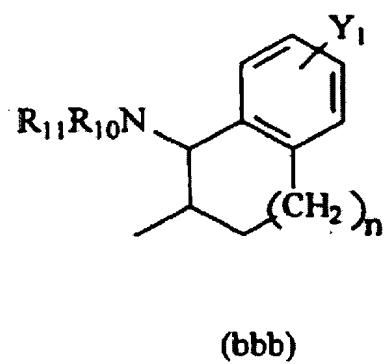
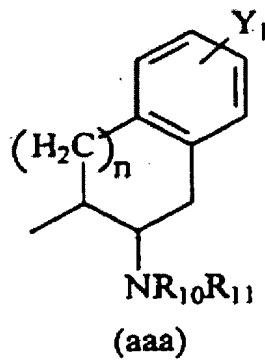
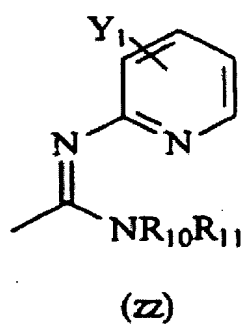
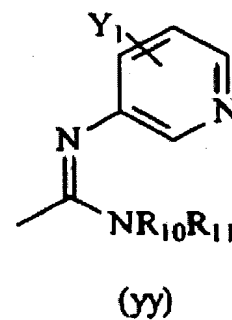
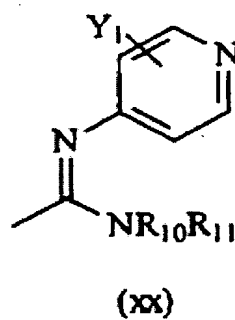
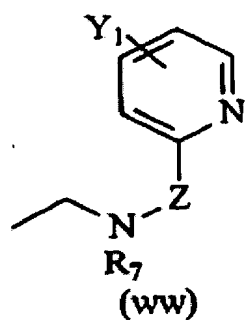
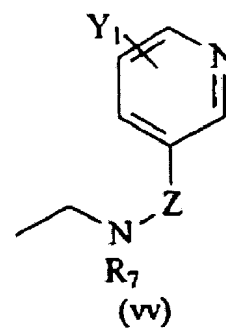
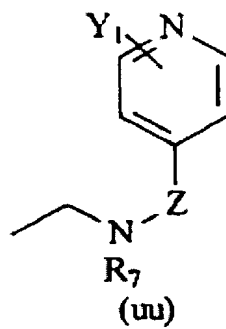
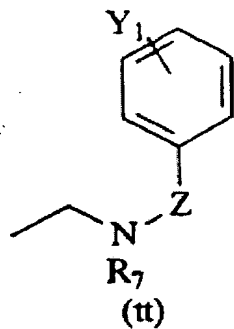


(ii)



(jj)





X₁ is hydrogen, C₁₋₈ alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

X₂ is hydrogen, C₁₋₈alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

or X₁ and X₂ together form =O, =S, or =NH;

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,
NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, CH₂(CH₂)_nY₂, or C(=NH)NR₁₆R₁₇;

R₈ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₉ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₀ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₁ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₂ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₃ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₄ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₅ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₆ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl; and

R₁₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl

and pharmaceutically acceptable salts thereof.

Claim 8 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z , n , X_1 , X_2 , and R_7 - R_{17} are as in Claim 7;

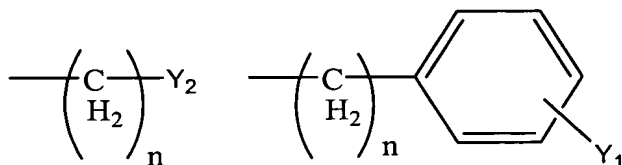
Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkynyl, C_{3-8} alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(w) and (cc).

Claim 9 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1 , Y_2 , R_4 , R_5 , Z , n , X_1 , X_2 and R_8 - R_{15} are as in Claim 7;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 10 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{15} are as in Claim 7;

R₁ is C₁₋₈ alkyl;

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄,
CH₂OH, CH₂OR₈, or COCH₂R₉;

Y₃ is H;

R₂ and R₃ are each, independently, H or methyl, wherein R₂ and R₃ cannot both be H
at the same time;

R₄ is H, C₁₋₈ alkyl, CO₂C₁₋₈alkyl, or CH₂ aryl substituted by one or more substituents
Y₁ and the stereocenter adjacent to R₄ is in an (S) configuration;

R₅ is H, C₁₋₈ alkyl, CH₂CO₂C₁₋₈ alkyl;

R₆ is a group having a formula selected from the group consisting of structures (a)-(c)
and (h)-(o); and

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,
NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

Claim 11 (Previously Presented) The kappa opioid receptor antagonist compound of
claim 7, wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₄ are as in Claim 7;

R₁ is methyl,

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄,
CH₂OH, CH₂OR₈, or COCH₂R₉;

Y₃ is H;

R₂ and R₃ are each H or methyl, such that when R₂ is H, R₃ is methyl and vice versa;

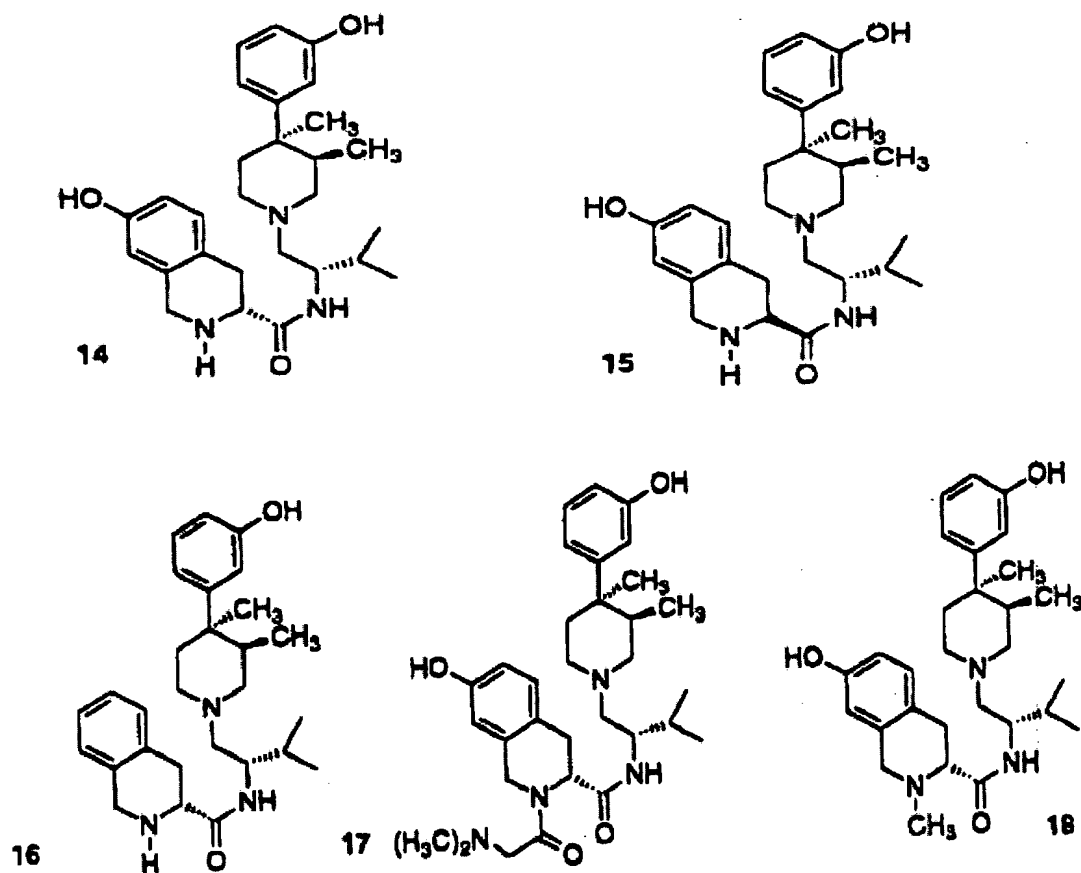
R₄ is C₁₋₈ alkyl, or CO₂C₂₋₈ alkyl, and the stereocenter adjacent to R₄ has a
configuration of (S);

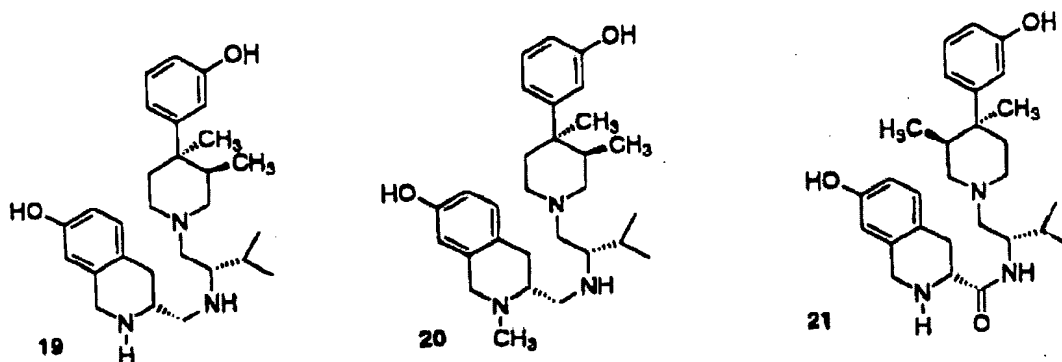
R₅ is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

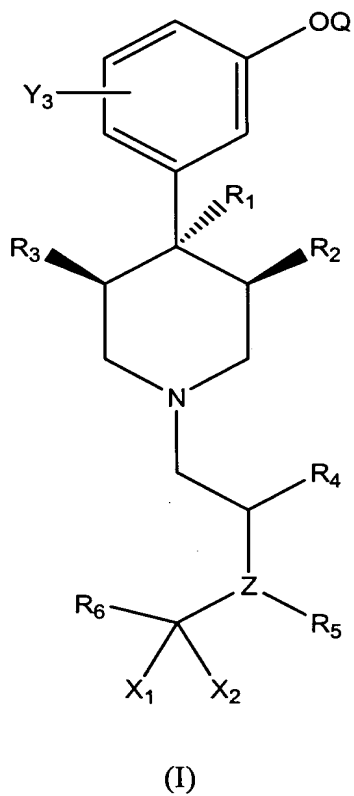
R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

Claim 12 (Previously Presented) The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae 14-21 as follows:



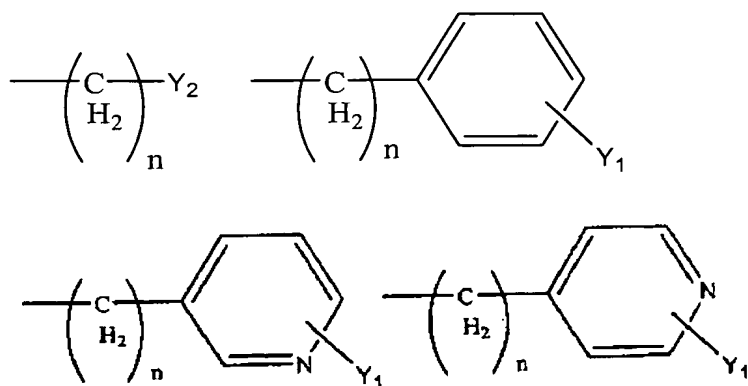


Claim 13 (Previously Presented) A pharmaceutical composition comprising:
 an effective amount of a kappa opioid receptor antagonist and a physiologically
 acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula
 (I):



wherein Q is H or COC₁₋₈ alkyl;

R₁ is C₁₋₈ alkyl, or one of the following structures:



Y_1 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_{11} , $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_3R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

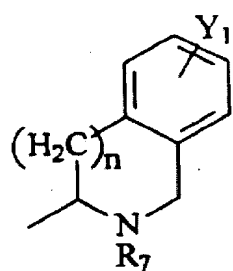
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 , or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S, there is no R_5

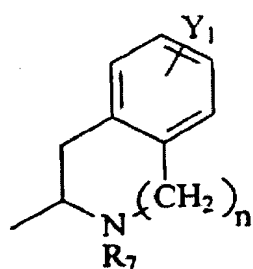
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

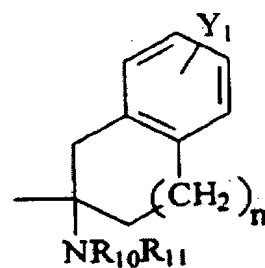
R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



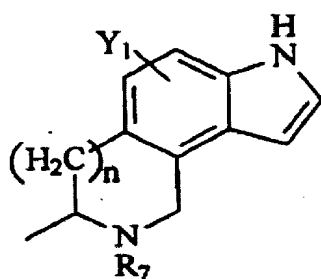
(a)



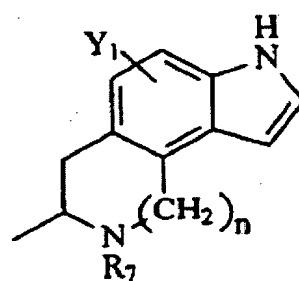
(b)



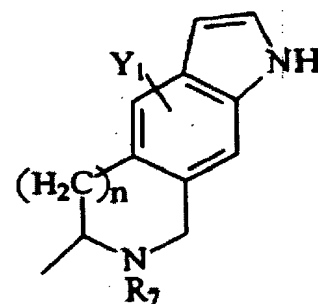
(c)



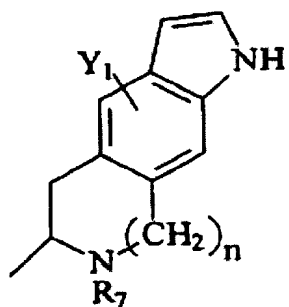
(d)



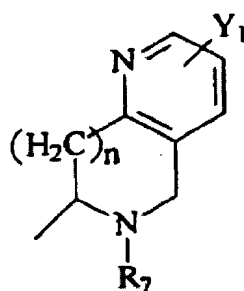
(e)



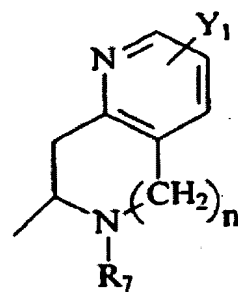
(f)



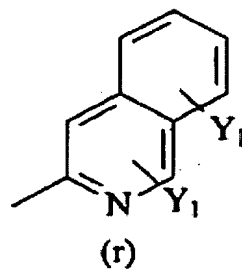
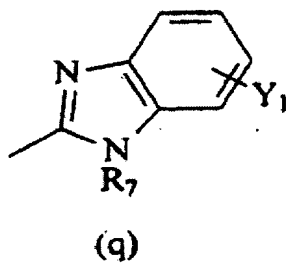
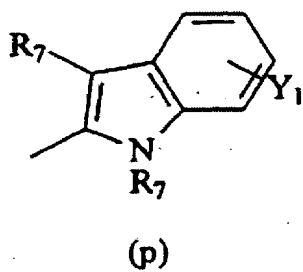
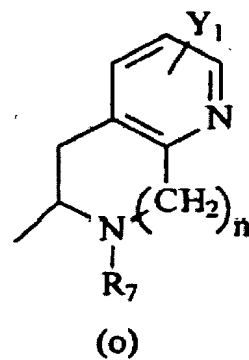
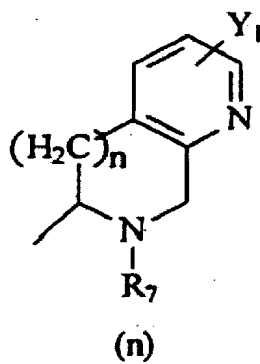
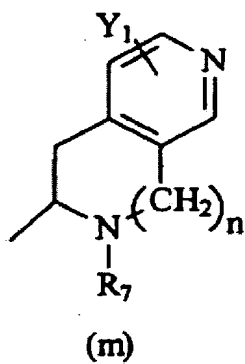
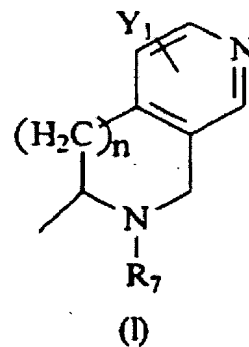
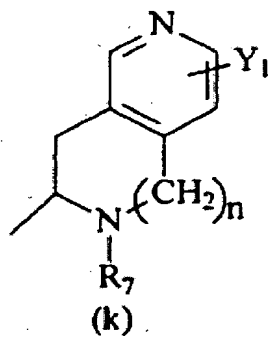
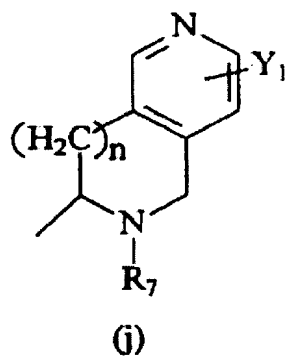
(g)

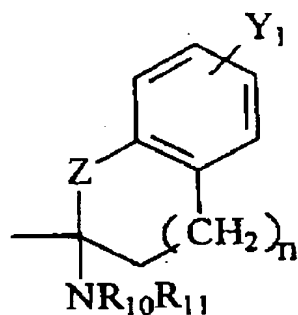


(h)

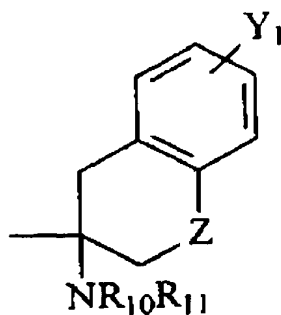


(i)

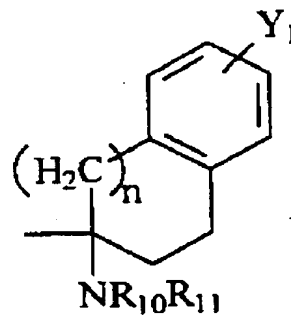




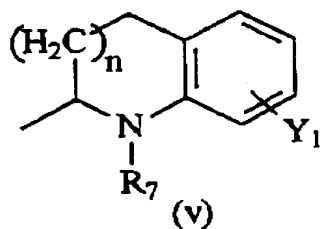
(s)



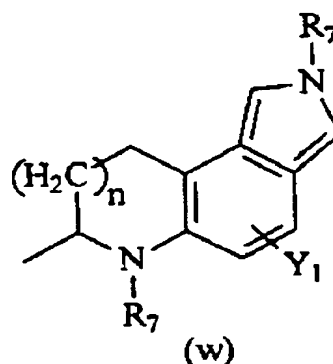
(t)



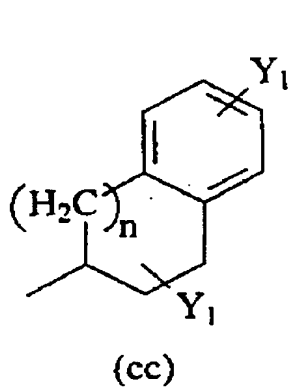
(u)



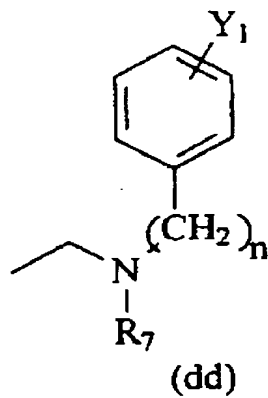
(v)



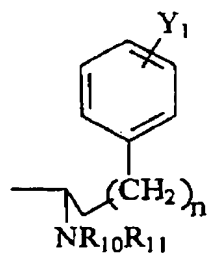
(w)



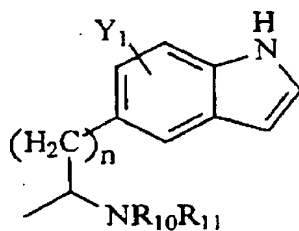
(cc)



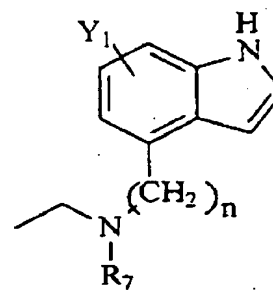
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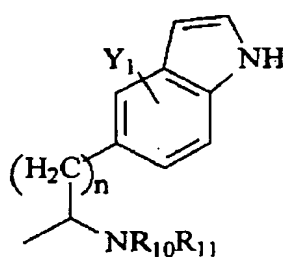
(ee)



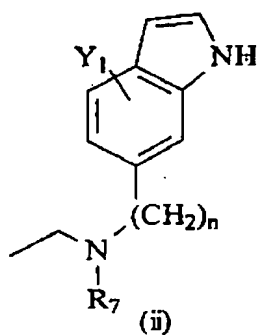
(ff)



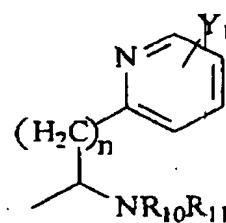
(gg)



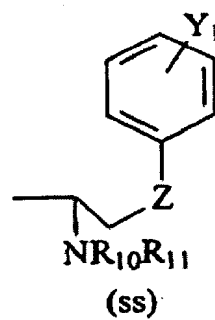
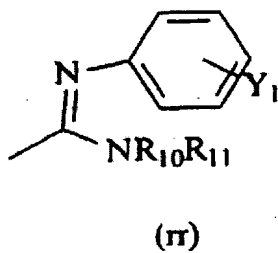
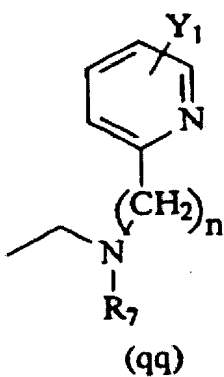
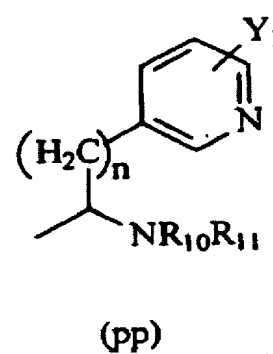
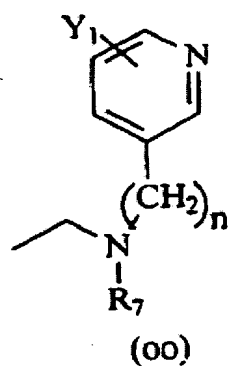
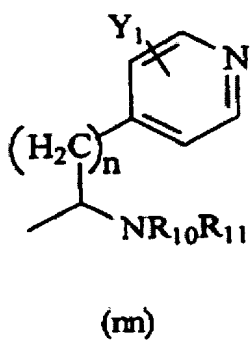
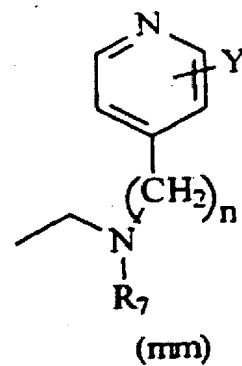
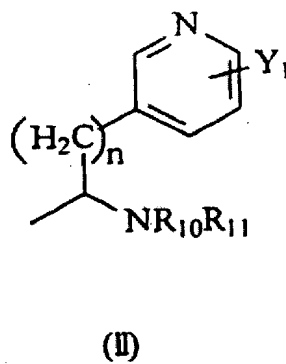
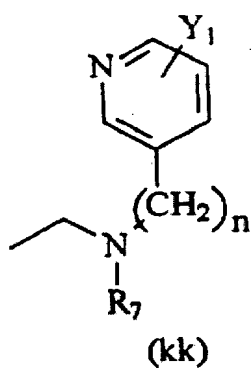
(hh)

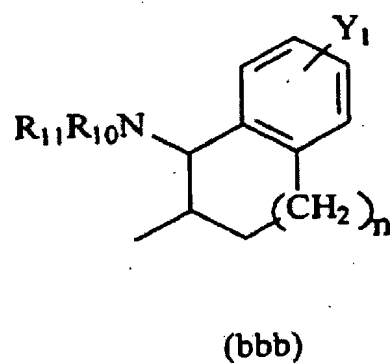
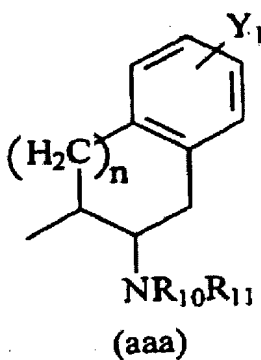
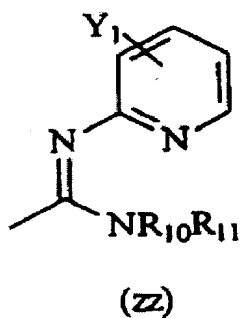
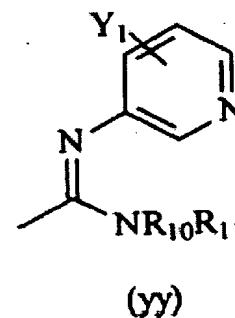
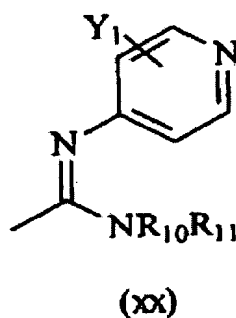
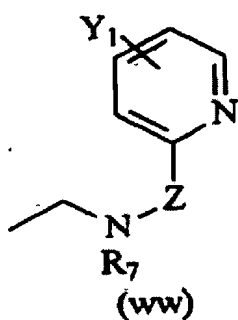
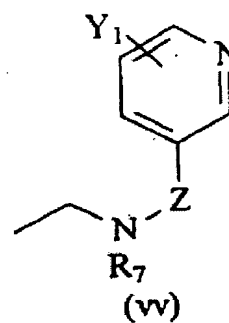
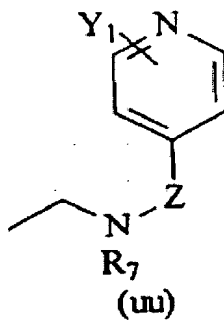
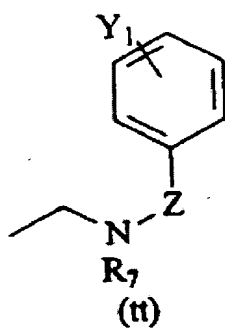


(ii)



(jj)





X₁ is hydrogen, C₁₋₈ alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

X₂ is hydrogen, C₁₋₈alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

or X₁ and X₂ together form =O, =S, =NH;

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,
NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, CH₂(CH₂)_nY₂, or C(=NH)NR₁₆R₁₇;

R₈ is H, C₁₋₈alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₉ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₀ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₁ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₂ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₃ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₄ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₅ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₆ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ; and

R₁₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂'; wherein Y₂' is H, CF₃, or C₁₋₆alkyl

or a pharmaceutically acceptable salt thereof.

Claim 14. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z , n , X_1 , X_2 , and R_7 - R_{17} are as in Claim 13;

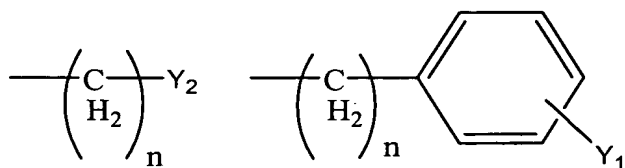
Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(w) and (cc).

Claim 15. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein Y_1 , Y_2 , R_4 , R_5 , Z , n , X_1 , X_2 and R_8 - R_{15} are as in Claim 13;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r) shown above; and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 16. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{15} are as noted- above in Claim 13;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 17. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{14} are as in Claim 13;

R_1 is methyl,

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

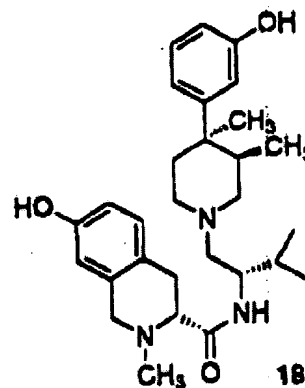
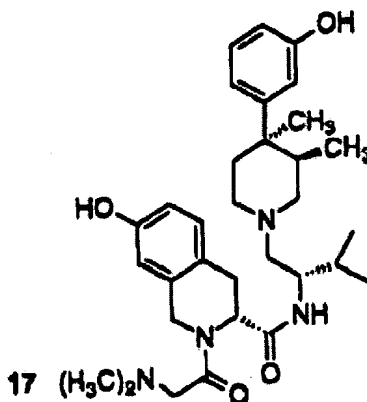
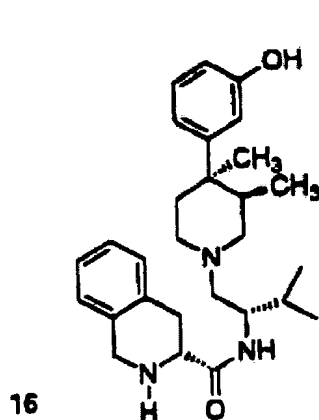
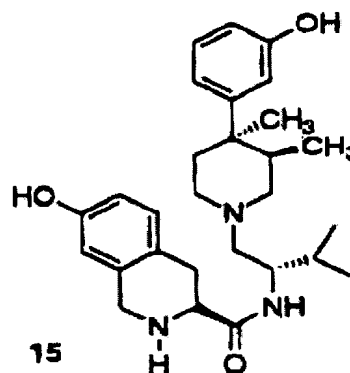
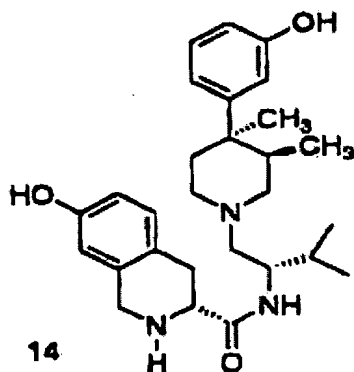
R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

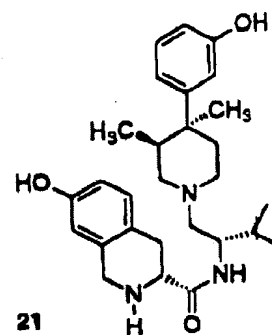
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

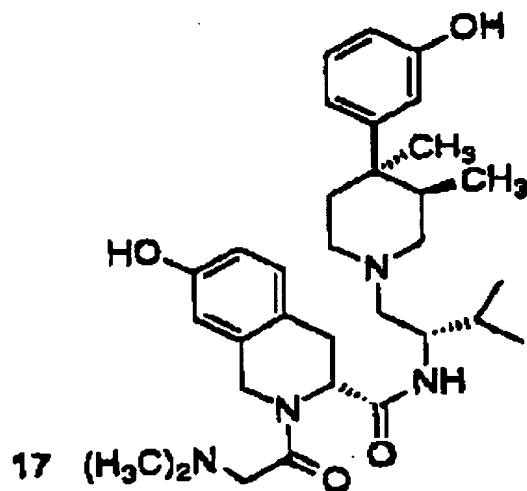
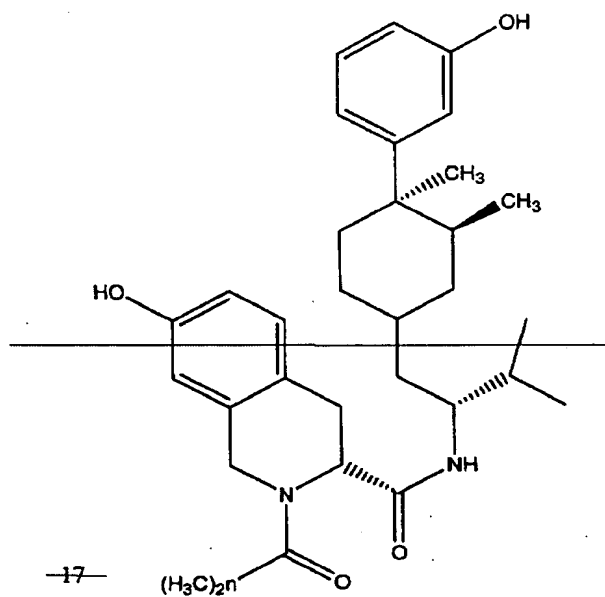
R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y, or $CH_2(CH_2)_nY_2$.

Claim 18. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 as follows:





Claim 22. (Currently Amended) The kappa opioid receptor antagonist according to Claim 7, having the chemical formula:



Claim 23. (Cancelled)

Claim 24. (Cancelled)

Claim 25. (Cancelled)